GAMETOCYTE PRODUCTION IN PATIENTS OF FALCIPARUM -- MALARIA TREATED WITH FANSIDAR.

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ABSTRAK

Telah dilakukan penelitian tentang produksi gametosit dari *P. falciparum* secara *in-vivo* di Batang, Jawa Tengah. Hasil penelitian ini menunjukkan bahwa jumlah rata-rata gametosit sebelum diobati dengan Fansidar adalah 75 per ml darah, dan jumlah rata-rata pada hari 7 sesudah diobati adalah 654 per ml darah. Hal ini berarti bahwa perbandingan jumlah rata-rata sesudah : sebelum pengobatan adalah 8,7 : 1.

Gametosit yang terbentuk sesudah pengobatan ini ternyata infektif untuk nyamuk *Anopheles aconitus* yang digigitkan pada volunteer, dan menghasilkan sporosoit pada hari 15—16 sesudah di-infeksikan. Hasil tersebut menunjukkan bahwa pengobatan menggunakan Fansidar saja, akan dapat meningkatkan transmisi malaria falciparum.

INTRODUCTION

Chloroquine resistant *Plasmodium falciparum* has been found throughout South East Asia, including Indonesia.
It has been found in 22 out of 27 provinces in Indonesia and has become a big problem in Malaria Control Programme. As alternate chemotherapy, Fansidar and Fansidar-Mefloquine combination will be used.

Recently, Fansidar resistant *P. falciparum* has been reported from several South East Asian Countries, including reports from Irian Jaya and East Timor, Indonesia (1, 2).
Therefore, a study on resistancy of *P. falciparum* to Fansidar by *in-vivo* and *in-vitro* techniques has been conducted in some provinces in Indonesia, before Fansidar be widely used.
The data from the study on *in-vivo* Fansidar resistance of *P. falciparum* indicates that Fansidar treatment, while clearing asexual parasitemia, results in the production of large number of gametocytes, so that additional studies on production of gametocytes after Fansidar treatment had been conducted in the Batang district, Central Java, Indonesia, and the results are presented in this paper.

MATERIALS AND METHODS

Patients were included in this study only if they met the following criteria : aged above 2 years, not suffering from serious diseases, harbouring only malaria of *P. falciparum* species with parasitemia between 500 — 100,000 per ml of blood, had not taken any malarial drug(s) recently (tested by urine test, using Dill-Glazko for 4-aminoquinoline and Lignin for sulphonamides).

Fansidar was given as a single dose of 30 mg sulphadoxine per kg bodyweight. Blood smears were examined before treatment (day 0), and on 7 consecutive days. Giemsa stained blood smears were prepared by standard method, and the number of gametocytes were counted. This number was extrapolated to gametocyte per ml of blood based on average WBC count of 7,500 WBC/ml blood.

Potency of the gametocytes produced post treatment was assesed by experimental infection using *Anopheles aconitus* and volunteers. Twenty five laboratory-raised mosquitoes were fed on each volunteer and incubated at room temperature for 14—16 days to observe oocysts and sporozoites production.

RESULTS AND DISCUSSION

A total of 56 patients were treated with Fansidar. Mean values for gametocyte production are shown in Figure 1. On day 0, gametocyte number was 75 per ml and it was increasing daily until day 7 when it reached 8.7 times the number on day 0.

Bruce-Chwatt et al. (3), discussed the effect of pyrimethamine and sulphonamides on gametocytes, i.e.: pyrimethamine has no apparent effect on the number, morphology and production of gametocytes, but the action of the drug appear to inhibit subsequent sporogony in the mosquito, resulting in the decrease of transmission of infection within the community.

Sulphadoxine, the other component of Fansidar, may increase gametocyte production, however, these gametocytes may not be infective to mosquitoes. That is why those gametocytes will not develop into cysts or sporozoites.

Experimental infection of mosquitoes were done on 18 volunteers, pre and post treatment. Most of the mosquitoes died before cysts or sporozoites had been produced, except in 5 groups from 5 vollunteers. Oocysts were found from these 5 groups, but the mosquitoes died before sporozoites were produced.

Additional studies were conducted by infecting mosquitoes only after treatment of Fansidar. Oocysts and sporozoites were found in 5 out of 6 groups of mosquitoes, while the remaining groups could only be followed up to the oocyst stage. In all cases, oocysts were found on day 7—13 and sporozoites on day 15—16 post-infection.

The results suggest that gametocytes produced after Fansidar treatment remain capable of producing sporozoites in the mosquitoes.

These observation suggest that Fansidar treatment of *P. falciparum* infection appears to result in the production of large number of gametocytes capable of infecting mosquitoes vectors. This could create a situation of increased infection sources and increased transmission. Therefore, Fansidar should only be given in combination with a sporontocidal drug.

SUMMARY

P. falciparum gametocyte production after Fansidar treatment was studied *in-vivo* in the Batang District of Central Java. The results revealed a mean of 75 gametocytes per ml of blood before the treatment, and a mean of 654 per ml of blood on day 7 post treatment, it was giving a post-treatment : pre-treatment ratio of 8.7. Gametocytes produced after

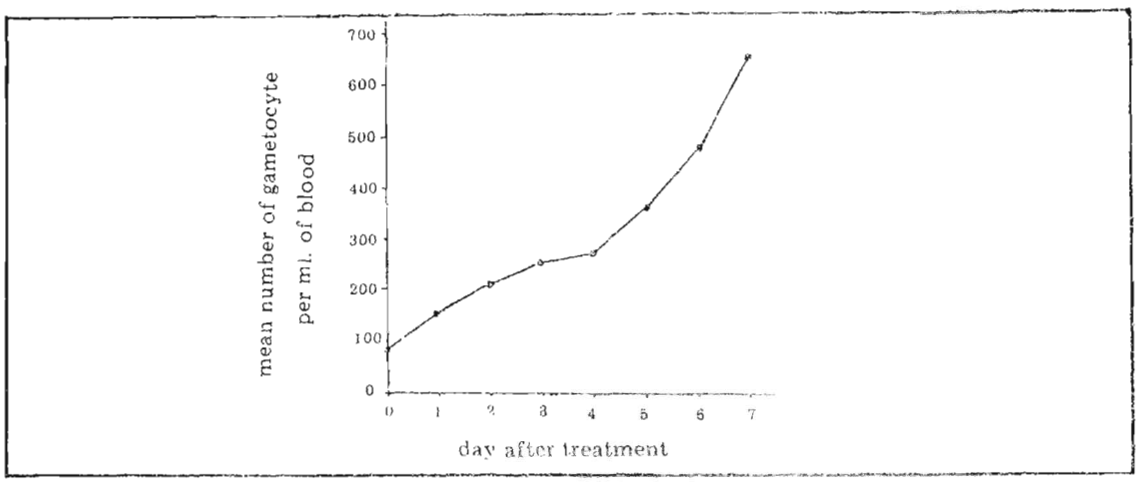

Figure 1. Mean number of gametocyte of *Plasmodium falciparum* after Fansidar treatment, in Batang, Central Java.

Fansidar treatment were infective to *A. aconitus* mosquitoes fed on volunteers, producing sporozoites at 15–16 days post-feeding. These results suggest that Fansidar treatment alone may increase transmission of *P. falciparum* malaria.

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